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# Technetium-99m stannous pyrophosphate scintigraphy in patients with calcification within the cardiac silhouette[1]

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SUMMARY Technetium-99m stannous pyrophosphate scintiscanning was performed in 22 patients with radiographically detected calcification within the cardiac silhouette. All but one of these scintigrams showed a localised area of increased activity similar to that ordinarily seen in acute myocardial infarction. Scintiscans in 3 patients after removal of the calcified aortic valve reverted to negative. It was concluded that this technique for acute infarct detection may yield false positive results in the presence of cardiac calcification.

Myocardial imaging with technetium-99m stannous pyrophosphate (99mTc-PYP) is being used frequently in the clinical diagnosis and localisation of acute myocardial infarction. Since its introduction by Bonte and co-workers (Bonte *et al.*, 1974; Parkey *et al.*, 1974; McLaughlin *et al.*, 1975), experience has been accumulating with the use of this agent and the sensitivity and specificity of the diagnostic technique. Its specificity has been found to be adversely influenced in a variety of settings in which positive scintiscans may be obtained in the known or inferred absence of acute myocardial infarction (Ahmad *et al.*, 1975; Berman *et al.*, 1975; Willerson *et al.*, 1975; Abdulla *et al.*, 1976; Ahmad *et al.*, 1976; DiCola *et al.*, 1976; Klein *et al.*, 1976; Pugh *et al.*, 1976; Ahmad *et al.*, 1977; Prasquier *et al.*, 1977; Righetti *et al.*, 1977) (Table 1). It is uncertain whether positive images in unstable angina (Willerson *et al.*, 1975; Abdulla *et al.*, 1976), transient exercise-induced ischaemia (Berman *et al.*, 1975), and direct current cardioversion (DiCola *et al.*, 1976; Pugh *et al.*, 1976) should be termed 'false positive' since there may be myocardial necrosis without reflection by the usual clinical (electrocardiographic or enzymatic) values. In this sense, it is possible that technetium imaging is a more sensitive index of myocardial cell injury than the classical tests (Willerson *et al.*, 1975). After coronary artery bypass surgery, scintiscans have been found to show areas with increased uptake at the site of the vent in the left ventricle created during surgery (Ahmad *et al.*, 1975). Left ventricular aneurysms and dyskinetic areas have also been found to be associated with positive scintiscans without evidence of acute myocardial infarction (Ahmad *et al.*, 1976, 1977). Scintiscans which are positive in the presence of impaired renal function or after left mastectomy (Prasquier *et al.*, 1977) may represent inadvertent blood pool scanning, with abnormal positivity being the result either of high levels of circulating tracer material or of diminution in shielding over the left thorax. Valvular calcification has been a controversial

Table 1 *Sources of false positive 99mTc pyrophosphate scans*

| *Source* | *Reference* |
|---|---|
| Unstable angina | Willerson *et al.* (1975), Abdulla *et al.* (1976) |
| Transient ischaemia | Berman *et al.* (1975) |
| DC cardioversion | DiCola *et al.* (1976), Pugh *et al.* (1976) |
| CAB surgery | Ahmad *et al.* (1975) |
| LV aneurysm | Ahmad *et al.* (1976), Ahmad *et al.* (1977) |
| LV dyskinesis | Ahmad *et al.* (1977) |
| Impaired renal function | Prasquier *et al.* (1977) |
| Left mastectomy | Prasquier *et al.* (1977) |
| Cardiac calcification | Klein *et al.* (1976) |

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source of false positive 99mTc-PYP scintiscans (Klein *et al.*, 1976; Righetti *et al.*, 1977), and this study was undertaken to determine whether (a) calcified structures within the cardiac silhouette take up 99mTc-PYP; and (b) the spatial distribution of this uptake allows it to be distinguished from that in acute myocardial infarction.

## Subjects and methods

Twenty-two patients with calcification within the cardiac silhouette shown either on plain chest *x*-ray or by fluoroscopy at cardiac catheterisation underwent 99mTc-PYP imaging. None of the patients in the study had clinical, electrocardiographic, or enzymatic evidence of acute myocardial infarction, preinfarction angina, or had undergone exercise testing or direct current cardioversion within one month preceding the study. Of the 22 patients, calcification was located in the aortic valve in 12, the mitral valve or annulus in 5, the pericardium in 3, within the myocardium in 1, and within the wall of the left anterior descending coronary artery in 1 (Table 2). Myocardial imaging was performed on a Conuclear gamma camera with a low energy parallel hole collimator 90 minutes after intravenous injection of 20 mCi 99mTc-PYP (New England Corporation). Images totalling 500 000 counts in the anterior, 45° left and right anterior oblique, and left lateral projections were recorded on Polaroid film and processed on a Gamma-11 computer (Digital Equipment Corporation). Computerised background subtraction and contrast enhancement were performed by previously described techniques (McLaughlin *et al.*, 1975). Analogue and processed images were analysed by 3 independent observers.

Table 2 *Localisation of calcification*

| *Site* | *No. of patients* | *No. visible on plain CXR* | *No. of positive scintigrams* |
|---|---|---|---|
| Aortic | 12 | 9 | 11 |
| Mitral | 5 | 3 | 5 |
| Pericardial | 3 | 3 | 3 |
| Myocardial | 1 | 0 | 1 |
| LAD* | 1 | 0 | 1 |
| Total | 22 | 15 | 21 |

*LAD, left anterior descending coronary artery.

Each observer assigned a grading of positivity ranging from 0 to 2. A scan was designated positive if the total score obtained by adding the 3 observers' scores was equal to or exceeded 4. In 3 patients, pre- and postoperative scans were obtained. In 1 patient who received 99mTc-PYP 60 minutes before surgical removal of the aortic valve the concentration of radioactivity in the removed valve was compared with that in the patient's blood using a scintillation well-counter.

## Results

Cardiac calcification visible on plain chest *x*-ray film in 15 of the 22 patients was seen in every patient with pericardial calcification and in most patients with aortic and mitral valvular calcification (Table 2). It should be pointed out, however, that this degree of radiographic recognition was attained retrospectively after calcification was detected and localised by fluoroscopy at the time of cardiac catheterisation. It is, therefore, not surprising that some areas of calcification which were later evident

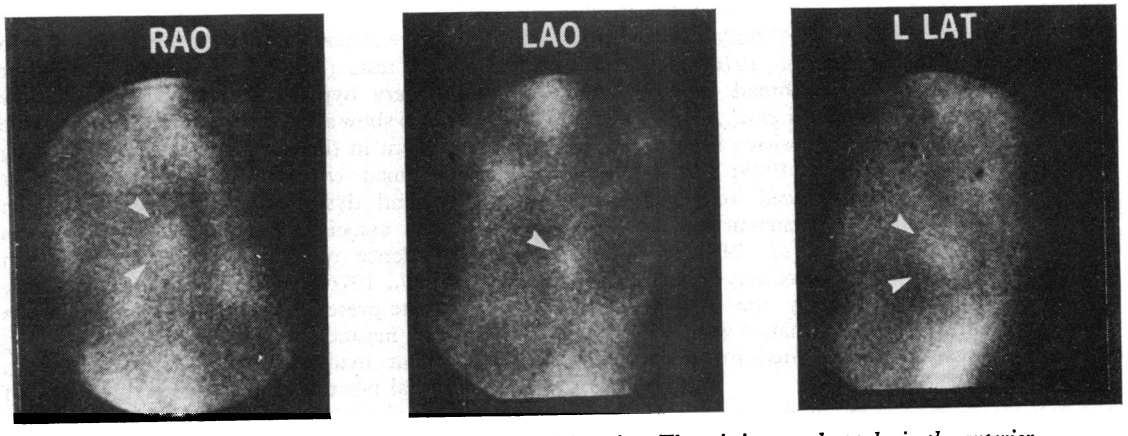


Fig. 1 *Scintigram from a patient with aortic valvular calcification. There is increased uptake in the anterior region as seen in the LAO view.*

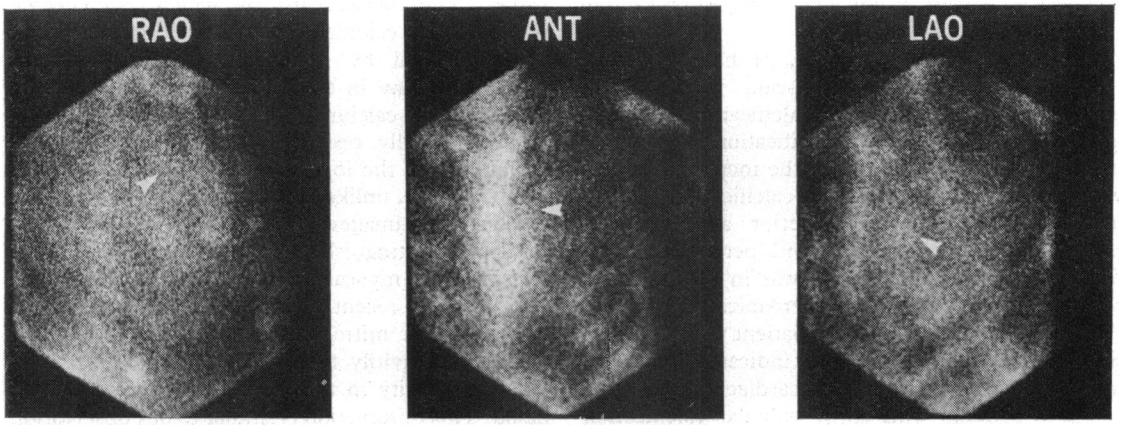


**Fig. 2** *Scintigram from a patient with mitral valvular calcification. The increased uptake in the inferoposterior region is clearly visible.*

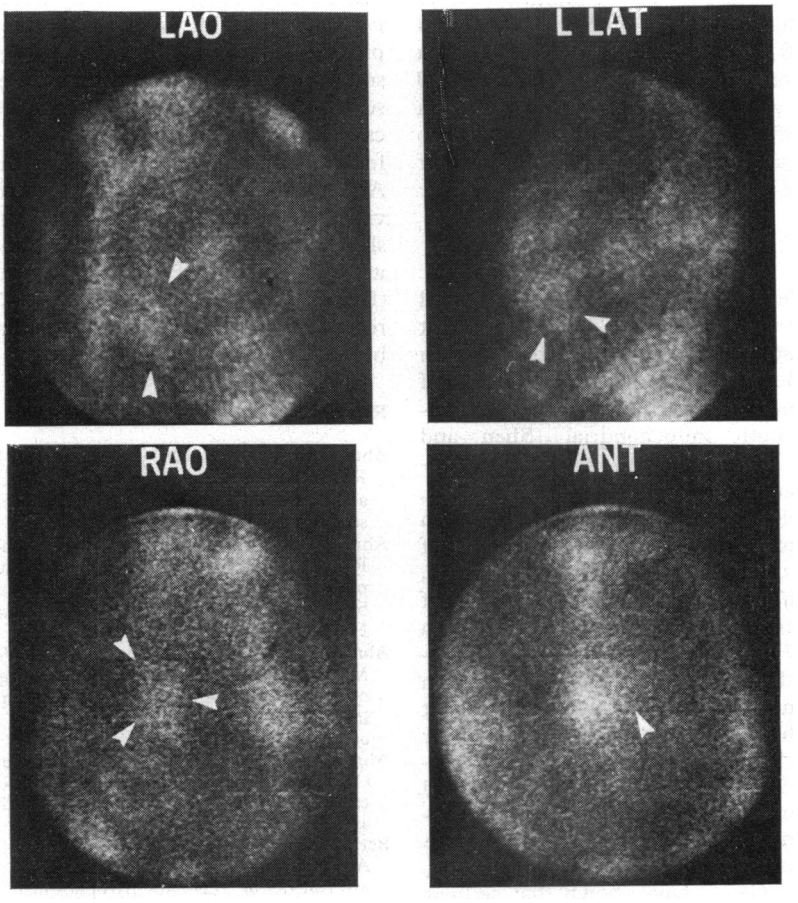


**Fig. 3** *Scintigrams from a patient with pericardial calcification. There is an area of localised increased uptake in the inferoapical region.*

on chest x-ray were originally undetected on routine radiological examination.

Of the 22 patients scanned, 21 had a positive technetium myocardial scintiscan, with only 1 patient with aortic valvular calcification having a negative scintiscan. When calcification was located in the aortic valvular region, the increased uptake was anterior (Fig. 1). Mitral calcification yielded increased uptake in the inferior and posterior regions (Fig. 2). In the cases with pericardial calcification, the increased uptake was in the posterior region in 2 patients and inferoapical in a third (Fig. 3). The images from the patient with calcification within the myocardium indicated increased uptake in the inferoposterior cardiac region.

Three patients with aortic valvular calcification undergoing aortic valve replacement had pre- and postoperative imaging. The increased uptake in the anterior region seen preoperatively in these patients was not seen after removal of the valve. One of these patients received 99mTc-PYP 60 minutes before the removal of the aortic valve. The valve was found to contain 34 500 counts/min per g compared with a simultaneous blood sample which contained 7900 counts/min per g as determined in a scintillation counter. This difference in activity was deemed to be more than adequate to generate an area of increased uptake on the scintiscan.

## Discussion

The uptake of 99mTc-PYP by irreversibly damaged myocardial cells has been found to bear a direct temporal and spatial relation to intracellular calcium accumulation (Buja *et al.*, 1975). The exact site of intracellular uptake has been the subject of controversy with both mitochondrial (Shen and Jennings, 1972; Buja *et al.*, 1975) and extramitochondrial (Dewanjee *et al.*, 1975; Coleman *et al.*, 1977) sites implicated. Calcium accumulation in necrotic myocardial cells may take the form of hydroxyapatite crystals (D'Agostino and Chiga, 1970; Buja *et al.*, 1975). Though the binding of pyrophosphate to hydroxyapatite is well known (Jung *et al.*, 1973), 99mTc-PYP uptake into irreversibly damaged myocardial cells has been shown to occur even in calcium-free medium (Schelbert *et al.*, 1976). Thus, technetium uptake can occur independently of hydroxyapatite formation (Dewanjee *et al.*, 1975; Schelbert *et al.*, 1976) and denatured macromolecules may bind technetium-chelate in a manner similar to pseudocalcification in other pathological mineralisation (Dewanjee *et al.*, 1975). Kim *et al.* (1971) have shown that cellular degradation products of fibrocytes were the site of dystrophic calcification in aging human aortic valves. The mechanisms by which 99mTc-PYP is taken up by calcified structures within the cardiac silhouette and by myocardial necrosis may be similar and may in both instances be unrelated to mitochondrial calcium uptake. Because the calcification is spatially restricted, the three-dimensional localisation of the increased isotope uptake is focal and, therefore, unlike other sources of false positive 99mTc-PYP images (Prasquier *et al.*, 1977), it cannot be distinguished from the uptake normally seen in acute myocardial infarction. Righetti *et al.* (1977) have recently shown that the calcified portions of a mitral valve took up 99mTc-PYP much more avidly than the fibrotic portions and that the activity in the valve far exceeded that in blood. This observation is similar to our observation of increased uptake by the calcified aortic valve of one of our patients.

Our studies indicate that calcification of structures within the cardiac silhouette can yield false positive 99mTc-PYP images. In many instances the calcification was visible on plain chest x-ray and should provide a means of pre-identifying this potential source of error. If the significance of a positive scintiscan is unclear because of the presence of cardiac calcification, a repeat study should be performed 10 to 14 days later to settle the question. Assuming that a reinfarction or extension of previous infarction is unlikely, the second scintiscan should be negative if the original increased uptake was the result of acute myocardial infarction (Parkey *et al.*, 1974; Buja *et al.*, 1975) but should remain positive if the increased uptake was caused by calcification.

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